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Efficacy of diffusion-weighted magnetic resonance imaging in the diagnosis and staging of endometrial tumors☆

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MR imaging;
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Abstract
Purpose: The goal of this study was to evaluate the efficacy of diffusion-weighted imaging (DWI) in differentiating between benign and malignant endometrial lesions and determinining tumor grade. It also aimed to determine the contribution of the DWI to the diagnosis by detection of the myometrial invasion depth in malignant lesions.
Materials and methods: The lesions were classified as benign ($n = 14$) or malignant ($n = 42$) according to the histopathological results and, the mean apparent diffusion coefficent (ADC) values were compared. For determining the myometrial invasion depth of malignant lesions, T2W, DWI and dynamic contrast-enhanced T1-weighted images (DCET1WI) were evaluated individually.
Results: The sensitivity, specificity and area under the curve for discriminating between malignant and benign lesions by using cutoff ADC value of 1.10×10^{-3} s/mm^2 were 85.7%, 92.8% and 0.95, respectively. According to the histopathological grading, there was no difference for the mean ADC values. For both observers the diagnostic accuracy of MRI in determining the depth of myometrial invasion in malignant lesions was found to be 87.1%, 89.7% and 76.9%, 76.9% for T2WI-DWI and DCET1WI, respectively.

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Conclusion: DWI and ADC measurements can accurately discriminate endometrial cavity lesions as benign or malignant. T2WI-DWI is highly effective in determining the depth of myometrial invasion.

In endometrial cancer, the disease stage, the depth of myometrial invasion of the tumor, and the histological grade are important factors, which determine prognosis and treatment. Histological grade is associated with the degree of differentiation of the tumor. As well as myometrial invasion, pelvic and para-aortic lymph node metastasis, tumor grade is directly associated with adnexal metastasis, positive peritoneal cytology, local recurrence and hematogenous spread [1]. In the high-grade tumors with deep myometrial invasion, in addition to total abdominal hysterectomy and bilateral salpingo-oophorectomy, lymph node dissection is performed and, in some patients, preoperative radiotherapy is applied [2]. These prognostic factors should be evaluated in the preoperative period in order to determine the appropriate treatment protocol.

Magnetic resonance imaging (MRI) is an ideal imaging modality for pelvic examination and known as the most accurate modality for the evaluation of endometrial pathology in the pretreatment period. Due to the fact that the signal intensity of a small tumor in MRI may resemble that of a normal endometrium rather than a endometrial tumor, the accuracy of imaging of the tumor may be constrained. A focal mass in T2-weighted (T2W) images may appear similar to the submucosal degenerated leiomyoma, adenomatous hyperplasia and hemorrhage within the cavity. The contrast between tumor and normal endometrium is pronounced with administration of Gadolinium-DTPA and it becomes possible to distinguish the small tumors [3]. However, due to concomitant myomas, in cases where the endometrial cavity is depressed or in the presence of adenomyosis, diagnostic difficulties may arise. Again, in patients with contrast agent allergy or impaired renal function, imaging methods, which can be an alternative to examination with contrast material, are needed.

Diffusion-weighted imaging (DWI) is becoming a part of the standard imaging protocols for the assessment of the female pelvic region, in recent years [4]. The image contrasts in DWI are a result of changes in the diffusion of water molecules in tissues. Malignant tumors are composed of tumor cells which are randomly organized and created an intense group. This effect prevents the free movement of water molecules, causing diffusion limitation. In the studies performed in recent years, it has been shown that the apparent diffusion coefficent (ADC) value in malignant lesions detected in the endometrial cavity were significantly lower than in benign lesions and normal tissue [5,6]. In different studies, it has been reported that DWI can replace dynamic contrast-enhanced T1-weighted (DCET1W) images in the assessment of myometrial invasion and can be used with T2W images in routine [7,8].

The study aimed to evaluate the efficacy of DWI in the differentiation of benign and malignant lesions of the endometrial cavity and the determination of tumor grade. It also aimed to determine the contribution of the DWI to the diagnosis by detection of the myometrial invasion depth in malignant lesions.

Materials and methods

Patients

The study group was created with patients with prediagnosis of endometrial pathology at the department of obstetrics and gynecology, between June 2010 and August 2011 and whose gynecologic pelvic MRI indicated the need for gynecological evaluation. The patients on whom dilatation and curettage (D & C) was performed before MRI and therefore whose cavities was filled with hemorrhagic content were excluded from the study. The patients with permanent ferromagnetic prosthesis implantation and those who displayed sensitivity to the paramagnetic contrast agents which were reported due to MRI examinations made previously were excluded from the study group. This prospective study was approved by the hospital ethics committee. Informed consent was obtained from all subjects included in the study.

A total of 56 patients between the ages of 35—86 (mean 56.0 ± 12.8 years) who were subjected to MRI with the prediagnosis of endometrial pathology and had lesions detected within the endometrial cavity were included in the study. The final diagnoses of the patients were based on the histopathological results of the materials obtained after surgery and/or D & C.

Technique

All MR examinations were performed on a 1.5-tesla (Siemens Magnetom Symphony Quantum, Erlangen, Germany) MRI device with a six-channel phased-array coil. Lower abdominal MR imaging protocols were created with the following sequences: the coronal True-FISP (TR/TE: 4.30 ms/2.15 ms, slice thickness: 5 mm, field of view [FOV]: 450 mm, matrix 256×90, flip angle [FA]: 780, number of signal averages [NEX]: 1), and axial and sagittal T2W TSE sequence was obtained (TR/TE: 4970 ms/97 ms, slice thickness: 3 mm, FOV: 280 mm, matrix 256×60, FA: 1500, NEX: 4). Before contrast administration, T1W flash 2D axial sequence (TR/TE: 173 ms/2.35 ms, slice thickness: 5 mm, FOV: 500 mm, matrix 256×70, FA: 700, NEX: 1) after contrast administration, T1W flash 3D axial [T1W flash 3D VIBE]

fat-suppressed (TR/TE: 6.61 ms/2: 37 ms, slice thickness: 2.5 mm, FOV: 500 mm, matrix 256 × 60, FA: 150, NEX: 1) sequence were obtained in the 30th and 60th seconds, as two phases. An intravenous contrast agent was administered via an automatic injection device with a speed of 3 ml/s. Immediately after the contrast agent, 20 cc of saline was administered.

DWI was performed prior to contrast-enhanced sections. The technical parameters were TR/TE: 3300 ms/93 ms, slice thickness: 5 mm, FOV: 400 mm, matrix 128 × 100, NEX: 3. The diffusion-weighted sequences were obtained in the axial plane, each of the 3 directions to SSEP-SE T2 (x, y, z), in different b values (0, 400, 800 s/mm^2) by applying diffusion-sensitive gradients. Isotropic images consisted of the images created by the device by taking the cube root of multiplying of signal intensity measured in x, y, z directions and eliminating the signal changes depending on the direction. ADC maps belonging to isotropic images of b = 400 and 800 s/mm^2 values were created automatically by the device and the mean ADC values of all lesions were measured through these maps.

Image analysis

The morphological features and signal intensity of the endometrial cavity lesions seen on T2W and DWI and the contrasting characteristics of them in DCET1W images were evaluated. Then all the diffusion-weighted imaging sets were transferred to a different workstation to carry out the ADC measurements (Leonardo console, software version 2.0, Siemens, GERMANY). In all lesions, on ADC maps, ADC measurements were performed on the circular region of interest (ROI) placed on the lesion, from the widest part of the lesion. Before the ADC measurements, the widest part of the lesion was detected by examining T2W images and DWI obtained at the value of b = 400—800 s/mm^2. The places in the lesions, which showed increased diffusion or diffusion restriction, were put forward by evaluating ADC maps qualitatively. ADC measurements were performed from the solid parts of the lesions showing diffusion restriction or increased diffusion.

T2W and DWI were evaluated together in order to determine the depth of the myometrial invasion of malignant lesions. Image quality on T2W and DW images may not be standard. Evaluation of myometrial invasion can be difficult in cases with myometrial thinning due to postmenopausal changes or distention caused by tumor formed in the cavity and those with unclear transition zone. Evaluations were made by considering the image findings showing clear lesion boundaries. When DW images have inapropriate visual quality, T2W images were selected for assessment. Otherwise, when the assessment is not possible through T2W images due to abovementioned reasons, DW images were used for this puprose. Simultaneous assessment of the findings of T2W and DW images was defined as ''T2-DWI''. Then the images of each patient were randomly selected and, independently and fully blinded to the initial evaluation, evaluated with DCET1W images. Two radiologists (5 and 16 years experience in radiology, respectively) were independently assessed the depth of myometrial invasion of DCET1W and T2-DWI images which were obtained from all patients. DCET1W and T2-DWI images in a randomized order during two separate reading sessions. The observers were fully blinded. The depth of myometrial invasion were divided into 2 categories according to the FIGO staging system (FIGO, 2009). The presence of myometrial invasion limited to the endometrial cavity or less than 50% was considered to be as IA and the presence of equal to or more than 50% myometrial invasion was considered to be as IB. The widest area for each sequence that the tumor expanded into the myometrium was determined. At this level, the total myometrial thickness was measured and the invasion ratio was calculated. Diagnostic criteria for myometrial invasion, correlation of MRI findings to histopathology was done according to reported in previous studies [9,10] and showed in Table 1 and Fig. 1. Three patients with impaired kidney function who displayed a non-contrasting media administration could not be included in the evaluation to determine the depth of myometrial invasion.

Statistical analysis

All statistical analyses were performed using SPSS (Statistical Package for Social Sciences 13.0). Age and ADC values were given as mean ± standard deviation, with minimum and maximum values. After the mean ADC values of benign and malignant lesions of the endometrial cavity had been calculated, the Mann-Whitney *U* test was used for comparisons between groups. The mean ADC values of malignant lesions were calculated according to histological grading and the Oneway Anova test was used to compare between grade types. $P < 0.05$ was considered to be statistically significant. The Receiver Operating Characteristic (ROC) curve analysis was used to calculate the optimal cutoff ADC value, which can be used for the discrimination of malignant lesions from benign lesions. Sensitivity, specificity, positive predictive value (PPV) and negative predictive values (NPV) and AUC (Az) of DWI were calculated with a 95% confidence interval (CI). McNemar's test was used to determine the statistical discrepancy between two observers for both DCET1WI and T2-DWI. The kappa statistic was used to assess the agreement between two observers. Kappa values of 0.4 or lower indicate poor agreement, and those of 0.41—0.75 and greater than 0.75 indicate good and excellent agreement, respectively. With reference to the histopathological results

Table 1 MRI Criteria for the assessment of myometrial invasion.

Myometrial invasion	MRI findings
Intramucosal lesion	Continuous, noninterrupted junctional zone and subendometrial enhancement
< 50% superficial invasion	Disruption or irregularity of junctional zone and subendometrial enhancement
> 50% Deep invasion	Complete disruption of junctional zone subendometrial enhancement and signal intensity of tumor extends into outer half of myometrium

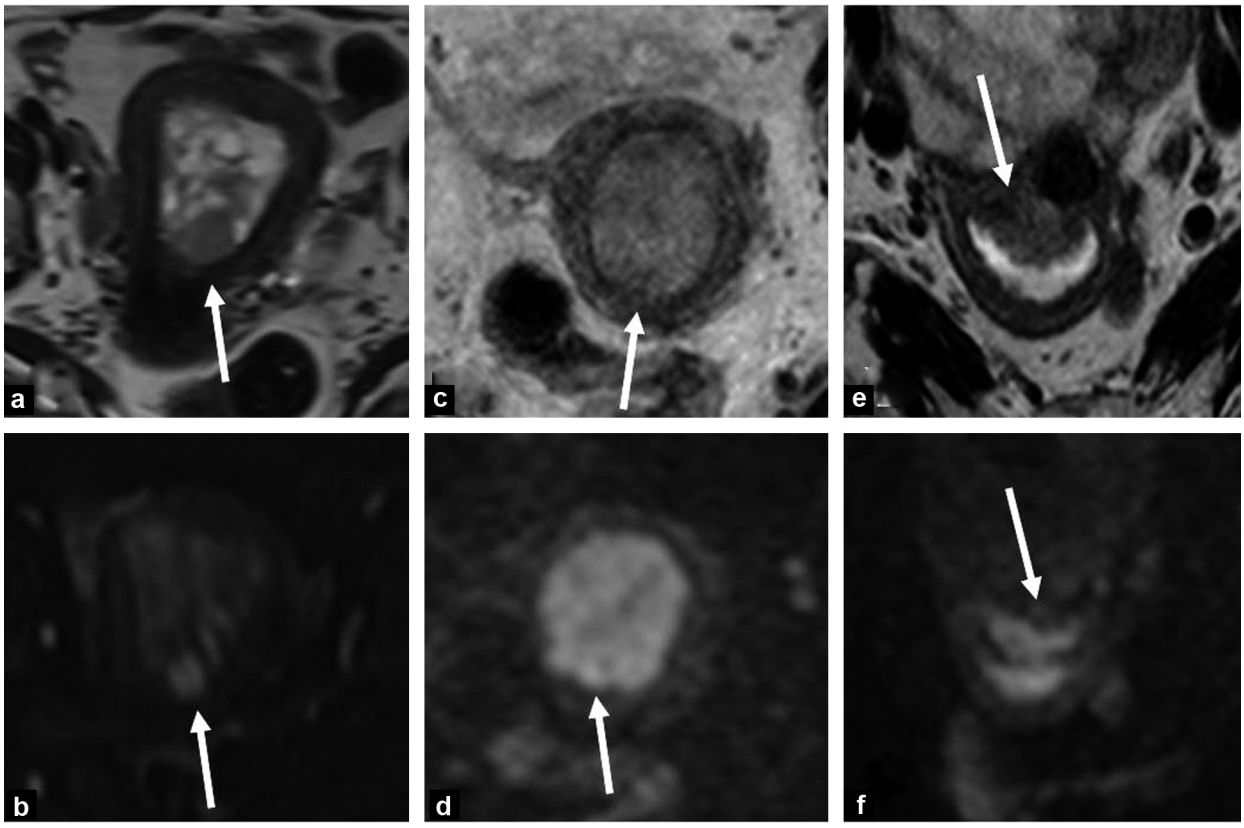

Figure 1. Axial T2-weighted and DW images show intramucosal lesion (a and b) continuous, noninterrupted junctional zone (arrows), superficial invasion (c and d) irregularity of junctional zone (arrows) and deep invasion (e and f) complete disruption of junctional zone (arrows).

for the determination of the depth of myometrial invasion, for each of the DCET1W, T2-DWI images, diagnostic accuracy, sensitivity, specificity, PPV, and NPV were calculated with 95% CI.

Results

Final diagnoses were obtained histopathologically in 42 patients after surgery, in 14 patients with D & C. They were classified as benign and malignant lesions according to the histopathological results. Forty of the 42 lesions, which were classified as malignant, were endometrial carcinoma and two of them were carcinosarcoma. The classification based on histological subtypes of 42 malignant endometrial cavity lesions is shown in Table 2. Seven of the 14 lesions classified as benign were endometrial polyps, 5 of them were submucosal fibroids and 2 of them were endometrial hyperplasia. Size of lesions and size of ROI according to histopathological type are shown in Table 3.

Fifty-six lesions classified as benign and malignant were compared in terms of ADC values. The mean ADC values were calculated for malignant lesions and benign lesions as $0.94 \pm 0.18 \times 10^{-3}$ s/mm^2, and $1.45 \pm 0.22 \times 10^{-3}$ s/mm^2, respectively. The mean ADC values of malignant lesions were lower than the mean ADC values of benign lesions, and this difference was statistically significant ($P < 0.05$).

When serous-mixed type adenocarcinomas and carcinosarcomas (Fig. 2) which histopathological grade was not measured were excluded, the remaining 37 endometrioid adenocarcinoma (Fig. 3) were divided into subtypes based on histological grade (Table 4). In terms of the mean ADC values according to the tumor grade status, a significant difference between the groups was not determined (Anova test, $P = 0.284$).

The cutoff value of ADC which will be used to determine whether the lesions are malignant with ROC analysis was accepted to be 1.10×10^{-3} s/mm^2 and the sensitivity,

Table 2 Classification based on histopathological subtypes of malignant lesions.

Histopathological type	Histopathological subtype	Number of lesions (%)
Endometrial carcinoma	Endometrioid adenocarcinoma	37 (88.0)
	Serous adenocarcinoma	2 (4.8)
	Mixed type adenocarcinoma (undifferantiate + serous adenocarcinoma)	1 (2.4)
Carcinosarcoma	Mixed Mullerian tumor	2 (4.8)
Total		42 (100)

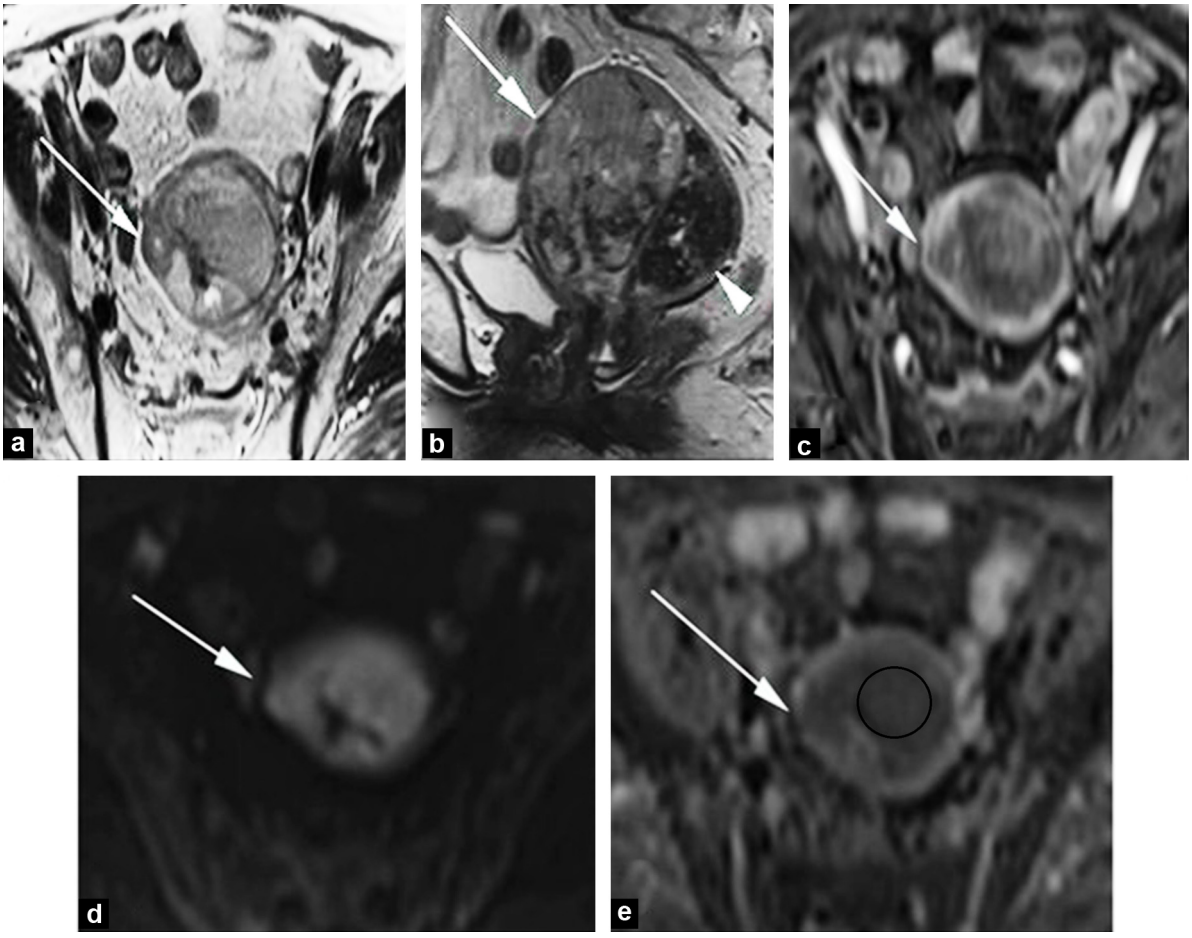

Figure 2. Axial (a) and sagittal (b) T2-weighted MR images show an 86-year-old patient with a diagnosis of a malignant mixed mullerian tumor. There is a mass (arrows) which fills and widens the endometrial cavity, it displays deep myometrial invasion in the right lateral, has slightly higher signal intensity than myometrium, its internal structure is heterogeneous and there is a myoma associated with it in the posterior (arrow head). On the dynamic contrast-enhanced T1-weighted image (c), the lesion defined in the cavity shows weaker contrast than myometrium and it is observed that it has signs of deep myometrial invasion (arrow). On the diffusion-weighted magnetic resonance image (d), the lesion has high signal intensity. On the ADC map (e), the lesion has low signal intensity, and displays diffusion restriction (arrows). The tumor boundaries are distinguished from the surrounding tissues clearly and it is observed that the lesion expands to the serosa especially in the right lateral. It has been confirmed histopathologically that the lesion, whose ADC value is measured as 0.83×10^{-3} s/mm^2, showed deep myometrial invasion.

Table 3 Size of lesion and size of ROI according to histopathological type.

Histopathological type	Size of lesion (cm)	Size of ROI (cm^2)
Endometrial polyp	2.6—8.5	2.34—6.93
Submucosal fibroid	2.7—14.4	2.09—18.56
Endometrial hyperplasia	2.2—4.3	2.05—3.61
Endometrial carcinoma	1.2—11.6	0.49—8.69
Carcinosarcoma	2.3—15.6	2.05—10.16

Table 4 Mean ADC values of endometrioid adenocarcinomas according to histological grading.

	Number of Lesions	Mean ADC value
Grade 1	16	0.91 ± 0.16
Grade 2	17	1.00 ± 0.21
Grade 3	4	0.87 ± 0.13

ADC: apparent diffusion coefficient (10^{-3} s/mm^2 $\pm$ SD).

specificity, PPV, NPV, Az were calculated to be 85.7%, 92.8%, 97.2%, and 68.4%, 0.95 respectively. There were overlaps in ADC values. There were 6 malignant lesions with ADC value over the cutoff and 1 benign lesion with ADC value under the cutoff (Table 5). The ADC value of benign lesion which was under the cutoff value was $1.06 \pm 0.05 \times 10^{-3}$ s/mm^2, and the histopathologic diagnosis was submucosal fibroids (Fig. 4). The ADC value of 6 malignant lesion whose ADC values are over the threshold value are changing between 1.13 and 1.32×10^{-3} s/mm^2, and all of their histopathological diagnosis was endometrioid type adenocarcinoma. In terms of depth of myometrial invasion, 3 of these cases were stage IA, other 3 cases were stage IB.

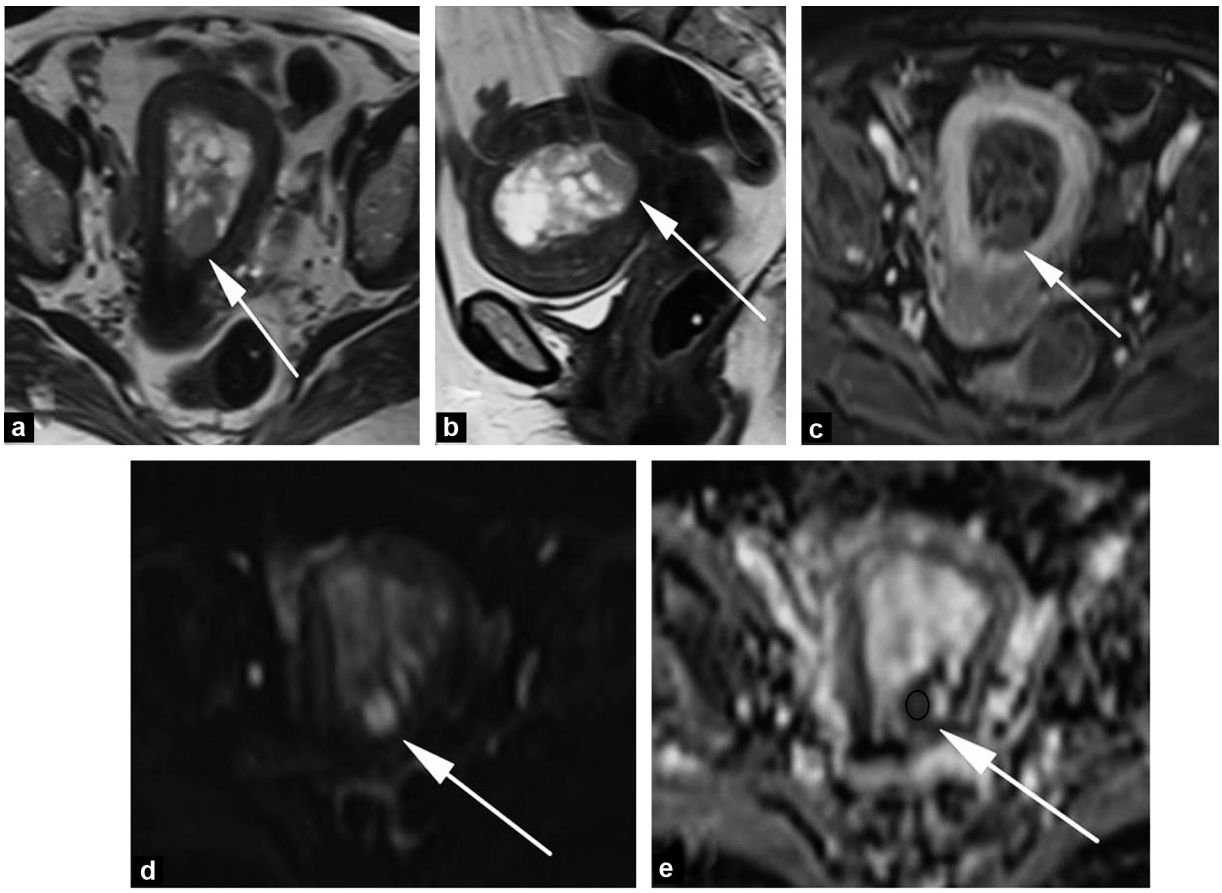

Figure 3. Axial (a) and sagittal (b) T2-weighted MR images show a 70-year-old patient diagnosed with endometrioid type adenocarcinoma histopathologically which has developed an endometrial polyp and is limited in the cavity; a mass, which is in the endometrial cavity, fills and widens the cavity, includes large cystic areas and slightly higher signal intensity areas, whose internal structures are heterogeneous. On the dynamic contrast-enhanced T1-weighted image (c), the lesion displays a weak heterogeneous enhancement. A diffusion-weighted magnetic resonance image (d) and ADC map (e) show the lesion which is defined in the endometrial cavity without diffusion restriction, except for an area in the posterior corpus showing focal diffusion restriction to which attention was called (arrows). In this area, it is evaluated as endometrial hyperplasia or the focus of tumor developing in the polyp, the ADC value was measured as 0.63×10^{-3} s/mm^2.

The depth of myometrial invasion was classified according to histopathological findings after surgery. Three of the 42 malignant lesions could not be included in the evaluation, which was performed to determine the depth of myometrial invasion due to the fact that contrast images could not be obtained. In 22 (56.4%) of the remaining 39 malignant lesions, tumors limited to the endometrial cavity, or myometrial invasion was less than 50% (IA). In the remaining 17 (43.6%) patients, myometrial invasion was equal to or more than 50% (IB). With reference of the histological results, for determination of the depth of myometrial invasion, the diagnostic accuracy of MRI was calculated separately for T2-DWI and DCET1W images. Diagnostic accuracy for T2-DWI for observer 1 and observer 2 were 87.1% (34/39) and 89.7% (35/39) respectively. No difference was observed between two observes with respect to T2-DWI evaluation ($P > 0.05$). The accuracy rate for DCET1W images was similar for observer 1 and observer 2 and was 76.9% (30/39). For T2-DWI and DCET1W images, the agreement between observers in assessing the determination of the depth of myometrial invasion was excellent (kappa values 0.88 and 1.00, respectively) (Table 6).

Discussion

Since DWI is a rapid and non-contrast technique that can provide qualitative and quantitative additional information to conventional MR sequences, it is increasingly used in the diagnosis of gynecological tumors in recent years. Additionally, DWI quality has improved with advanced techniques, thus the use of DWI is progressively increasing. However, due to the differences in the imaging sequences [half-Fourier acquisition single-shot turbo spin-echo (HASTE) or echo-planar imaging (EPI)], techniques [dual-source parallel radiofrequency (RF) transmission or conventional single-source transmission], echo time and the selected b values, optimal standardization is not achieved in ADC values [11]. There are some publications, which have demonstrated that DWI and ADC measurements can distinguish endometrial cancer from normal endometrium or benign pathologies with a higher rate of accuracy. In different studies, the mean ADC values of malignant lesions detected in endometrial cavity and benign lesions have been reported to range between 0.84 and 0.98×10^{-3} s/mm^2; 1.27 and 1.58×10^{-3} s/mm^2, respectively [5–7,12,13]. One of the

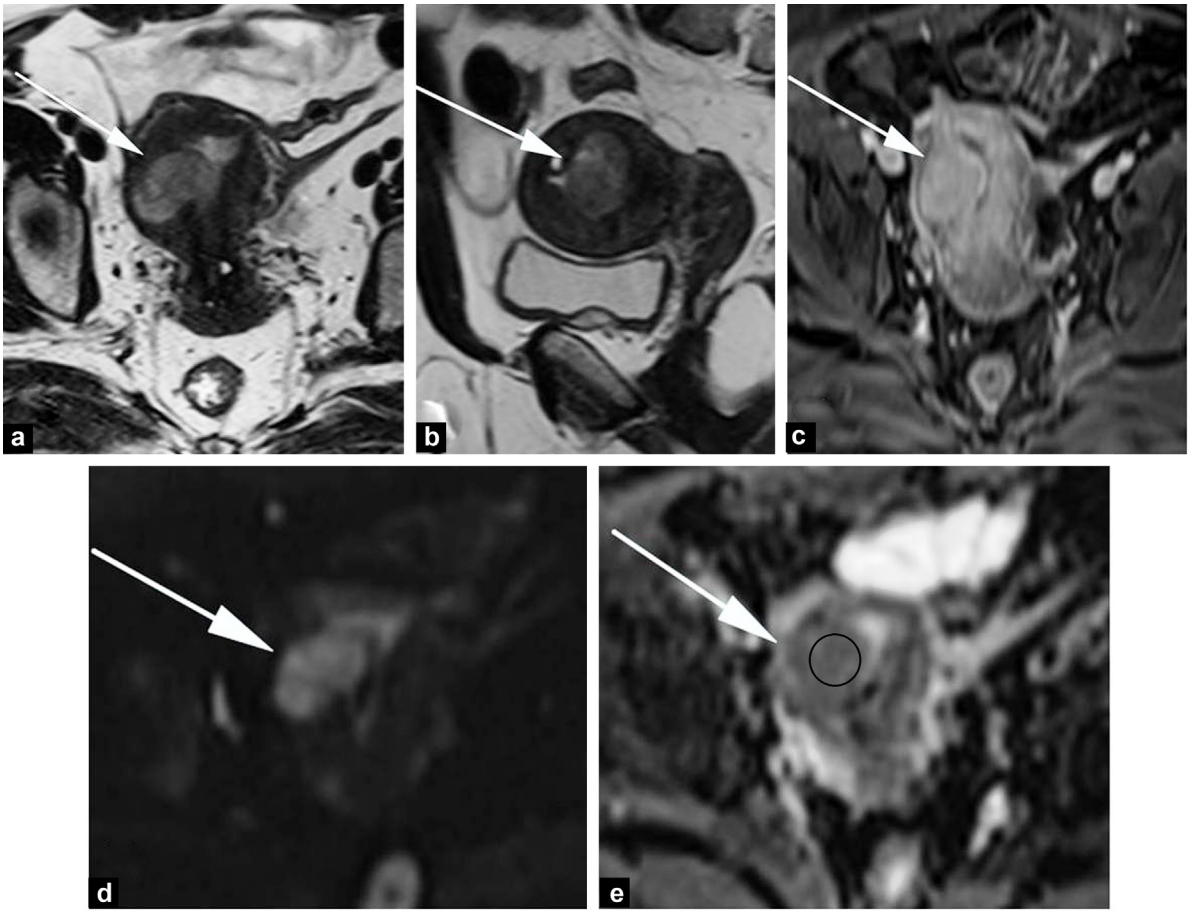

Figure 4. Axial (a) and sagittal (b) T2-weighted MR images show 55-year-old patient diagnosed histopathologically with a submucosal myoma, which extends into the right lateral myometrium in the endometrial cavity, with slightly high signal intensity. On the dynamic contrast-enhanced T1-weighted image (c), the same enhancement feature with the adjacent myometrium was observed (arrows). On the diffusion-weighted magnetic resonance image (d), the lesion has high signal intensity. On the ADC map (e), the lesion has low signal intensity, and showing diffusion restriction (arrows), its ADC value was calculated as 1.06×10^{-3} s/mm^2. However, taking into account the morphological and enhancement characteristics of the lesion, it was primarily thought to be a submucosal myoma.

reasons for the differences in ADC values in the studies is the use of different b value. Two different b values (400 and 800) were used in this study. However, as indicated by Ertürk et al. [14], because b value of 400 s/mm^2 represents tissue perfusion/diffusion, ADC value is over estimated than the expected and does not reflect the actual ADC value. Therefore, we performed measurements on ADC maps constituted with b = 800 s/mm^2. In all of these studies, it has been reported that, in terms of ADC values, there was a statistically significant difference between benign and malignant lesions. In our study, we found that the mean ADC value of the 42 malignant lesions ($0.94 \pm 0.18 \times 10^{-3}$ s/mm^2) of 56 lesions in total detected in endometrial cavity was statistically significantly lower than the mean ADC value of benign lesions ($1.45 \pm 0.22 \times 10^{-3}$ s/mm^2) ($P < 0.01$). Both in the light of the literature, as well as the findings of our study, it can be said that DWI and ADC measurements have a high diagnostic accuracy in the differentiation of the malignant lesions detected in the endometrial cavity than they do for benign lesions.

In our study, when the ADC threshold value used to determine whether the lesions are malignant was accepted as 1.10×10^{-3} s/mm^2, the sensitivity and specificity were 85.7%, 92.8%, respectively. There were overlaps in ADC values. There was one benign lesion whose ADC value was under the threshold value. The ADC value of this benign lesion was $1.06 \pm 0.05 \times 10^{-3}$ s/mm^2, and its histopathologic diagnosis was submucosal fibroids. Uterine leiomyomas are benign neoplasms occuring due to a combination of collagen and smooth muscle cells. ADC reflects the tissue properties such as extracellular field width, viscosity, cell density, type and shape and frequency of fiber [15—17]. The presence of homogeneous eosinophilic bands or plaque in the extracellular area caused by hyalinization led to a narrowing extracellular distance result and a decrease in the ADC value [18]. Submucosal myomas have different mean ADC values but they may overlap with malignant lesions [13]. The ADC value of 6 malignant lesions whose ADC values are over the threshold value varied between 1.13 and 1.32×10^{-3} s/mm^2, and all of their histopathological diagnosis was endometrioid type adenocarcinoma. Although six malignant lesions ADC values were over the threshold value, there was a high signal intensity in all DWI results and a lower signal intensity in the ADC series than normal endometrium. The lesions were also evaluated as malignant owing to T2W signal characteristics of the lesions, hypovascular lesions in the

Table 5 In cases of ADC values indicating overlap, clinical, histological and image findings.

Patient	Histopathological diagnosis	Depth of myometrial invasion[a]	ADC value[b], $\times 10^{-3}$ s/mm^2
1	Submucosal fibroids	Benign	1.06
2	Endometrioid type adenocarcinoma	IA	1.13
3	Endometrioid type adenocarcinoma	IA	1.15
4	Endometrioid type adenocarcinoma	IB	1.24
5	Endometrioid type adenocarcinoma	IB	1.27
6	Endometrioid type adenocarcinoma	IA	1.28
7	Endometrioid type adenocarcinoma	IB	1.32

[a] IA: myometrial invasion which is limited in the cavity or less than 50%; IB: myometrial invasion which is equal to or more than 50%.
[b] ADC values, which are above or below treshold ADC value (1.10×10^{-3} s/mm^2).

DCET1W images, associated cervical involvement or signs of myometrial invasion. For this reason, assessment should not be made only on the basis of the ADC measurements, the morphological characteristics of lesions in the conventional sequences should also be considered. The detection of small lesions in endometrial cavity and their characterisation are not always possible. Nowadays, when detected lesions in the endometrial cavity have myometrial invasion according to defined criteria in the MRI, the diagnosis of malignancy can be made. However it's difficult to evaluate microscopic (minimal) invasion by DWI and conventional sequences. In the situations such as ADC measurement is overlapping, the diagnosis can be made with only histopathological analysis. We consider that, with the use of; developing hardware, software, coil technology; new imaging sequences such as advancing scanning procedures in DWI, half-fourier acquisition single-shot turbo spin-echo; and new techniques such as dual-source parallel radiofrequency, minimal invasion can be detected in DWI or increased resolution conventional MRI.

In their study, Fujii et al. [5], found that when the threshold ADC value which will be used to determine whether the lesions are malignant was accepted as 1.15×10^{-3} s/mm^2, the ADC value of 2 of 11 endometrial carcinomas were defined as grade 1 owing to histopathological results, over the threshold value. For this reason, they argued that the relatively high ADC values of low-grade tumors can constitute a diagnostic trap. In our study, the histopathological results of 6 malignant lesions, whose ADC values were over the threshold value, were grade 1 for one of them and grade 2 for the remaining 5 of them. In the study conducted by Takeuchi et al. [7], the mean ADC values for grade 1 and grades 2–3 were $0.84 \pm 0.17 \times 10^{-3}$ s/mm^2, $0.71 \pm 0.17 \times 10^{-3}$ s/mm^2, respectively. In this study, the mean ADC value of grade 1 tumors were higher than that of grade 2–3 tumors, but there was no statistically significant difference. Bharwani et al. [19], in their study, performed tests in order to evaluate the contribution of DWI on the diagnosis in determining tumor grades in the endometrial carcinomas, for each calculated mean ADC values for each histologic types as $1.02 \pm 0.29 \times 10^{-3}$ s/mm^2 (grade 1), $0.88 \pm 0.39 \times 10^{-3}$ s/mm^2 (grade 2) and $0.94 \pm 0.32 \times 10^{-3}$ s/mm^2 (grade 3), respectively. Due to the fact that low-grade tumors include a lesser solid area than high-grade tumors, ADC values were expected to be higher. As a result of the study, due to the fact that there was a significant difference between grade of the tumor and mean ADC values, they emphasized that, in histological analysis, cellularity was not the only important factor for tumor grade, but that nuclear atypia was also an important factor, one which could not be evaluated by DWI for the purpose of determining the tumor grade. In our study, mean ADC values for each histological type of tumor were calculated as $0.91 \pm 0.16 \times 10^{-3}$ s/mm^2 (grade 1), $1.00 \pm 0.21 \times 10^{-3}$ s/mm^2 (grade 2), $0.87 \pm 0.13 \times 10^{-3}$ s/mm^2 (grade 3). There was no difference

Table 6 The diagnostic accuracy of T2-DWI and DCE T1W images in the evaluation of depth of myometrial invasion by reference to histopathological results.

	Observer 1		Observer 2						Kappa value (observer 1 vs. 2)	
	T2-DWI		DCET1W		T2-DWI		DCET1W		T2-DWI	DCET1W
Histopathological results	IA	IB	IA	IB	IA	IB	IA	IB		
IA[a]	22	0	22	0	22	0	22	0		
IB[b]	5	12	9	8	4	13	9	8		
Total	27	12	31	8	26	13	31	8	0.88	1.00

[a] IA: myometrial invasion which is limited in the cavity or less than 50%.
[b] IB: myometrial invasion which is equal to or more than 50%.

between the mean ADC values in terms of tumor grade. The results of this study, in contrast to the results of the study conducted by Fujii et al. [5], are similar to other data in the literature and support that, like cellularity, nuclear atypia is important in determining the tumor grade.

The gathering of information about myometrial invasion before the operation for the planning of treatment for endometrial cancer is important [20]. While the histopathology of a tumor can be determined with D & C preoperatively, the depth of myometrial invasion can be determined precisely in the postoperative period through pathologic examination of the specimen. In an earlier study, it was reported that MRI has a 87% sensitivity and 91% specificity in determining the depth of myometrial invasion of endometrial cancer [21]. Myometrial invasion is evaluated with the property that in T2W images, the tumor in the endometrial cavity has higher signal feature than the transition zone with low signal intensity, in DCET1W images, it is more hypovascular than the enhancing myometrium. In the presence of adenomyosis or in the cases of a thin myometrium or where the transition zone cannot be observed clearly, evaluating the myometrial invasion becomes difficult. Again, in the cases with contrast agent allergy or impaired renal function, alternative imaging techniques to DCET1W images are needed. Andreano et al.'s [22] systematic review showed high sensitivity and specificity for MR imaging in assessing deep myometrial invasion in endometrial cancer prior to surgery and that diagnostic accuracy parameters do not differ between DWI and DCET1W images. Gallego et al. [23] reported that ADC maps obtained from DWI images acquired before surgery make it possible to assess the depth of myometrial invasion in a similar way to that of the intraoperative frozen-section study, and with an accuracy superior to that of conventional sequences. Shen et al. [13] studied 21 cases of endometrial carcinoma in order to assess the depth of myometrial invasion and classified the lesions according to the histological results as: tumor which is limited to the endometrial cavity, IA; the presence of myometrial invasion less than 50%, IB; the presence of myometrial invasion more than 50%, IC. The diagnostic accuracy for DWI and DCET1W images was reported to be 61.9% and 71.4%, respectively. At the end of the study, they found that, DCET1W images had a higher degree of sensitivity in the evaluation of superficial myometrial invasion, reasoning that DWI had poor resolution relative to other sequences. In our study, the diagnostic accuracy for the evaluation of the depth of myometrial invasion is in contrast to the study conducted by Shen et al. [13] and similar to other data in the literature [7,8,23—25], as for both observers T2W-DWI (87.1%, 89.7%) is higher than DCET1W images (76.9%, 76.9%). In contrast to Shen et al. [13], the results of our study in the evaluation of superficial myometrial invasion showed that the sensitivity of DCET1W and T2W-DW images is 100%. For two observers, the presence of deep myometrial invasion has been identified correctly in sagittal T2W images in the three cases and confirmed by DWI. However, because of the fact that DCET1W images were obtained in the axial plane, the depth of invasion was estimated to be less than it actually was. In our study, DWI was obtained in the axial plane and the axial DWI assessment may be insufficient in such cases. We are in the opinion that obtaining DW images in both axial and sagittal plane, into thin slices perpendicular to the body, would make the evaluation more complementary. However, both Beddy et al.'s [24] study and ours revealed high accuracy results through axial images. Lin et al. [25], in a study conducted with a 3-T MR scanner used to assess the depth of myometrial invasion, found that T2W-DWI, which was combined with DWI with a high b value in order to provide anatomic details determined the depth of myometrial invasion with the highest accuracy. In our study, we evaluated T2W and DWI together in an attempt to resolve the inadequate anatomical resolution of DWI. The results of our study show that DWI assessed with T2W images has a high diagnostic accuracy in the evaluation of the depth of myometrial invasion, and can be applied as an alternative to DCET1W images.

Our study had some limitations. The first of these is the lack of benign pathologies detected in the endometrial cavity. Because the institution that we work at is the greatest reference hospital in this region, the patients with suspicious malignancy are usually referred to our hospital. Therefore, the number of benign cases in the study is limited. This causes high pretest-probability. Due in particular to the different histological structure of submucosal myomas, the features of DWI and ADC values may vary and may overlap with endometrial malignancies. Studies with a larger population are needed in this regard. Secondly, due to technical deficiencies, T2W and DWI images could not be established in the study. By evaluating of T2W-DWI together at the same time, an attempt was made to overcome this deficiency.

Conclusion

DWI and ADC measurements have high diagnostic accuracy in discrimination of benign and malignant lesions in endometrial cavity. DWI assessed with T2W images has a high diagnostic accuracy in the evaluation of the depth of myometrial invasion, and can be applied as an alternative to DCET1W images. Therefore, the addition of DWI to conventional MRI yields more accurate evaluations.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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